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CDC Health Advisory

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CDCHAN-

Cluster of Cases of Thrombotic Thrombocytopenic Purpura (TTP) Associated with Intravenous Nonmedical Use of Opana ER®

Summary

The Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA) are working with the Tennessee Department of Health on a cluster of at least 10 patients with thrombotic thrombocytopenic purpura (TTP) who have injected the opioid pain reliever, Opana ER® (oxymorphone extended-release) for nonmedical reasons since February, 2012. Investigation is ongoing.

This HAN notice provides information on the following:

- Status of the investigation
- Background on TTP and opioid analgesics
- Recommendations
- Case definition

Status of the investigation

On August 13, a nephrologist notified the Tennessee Department of Health (TN DOH) of a cluster of 3 cases of TTP in a small rural community in northeastern Tennessee. All patients had a history of intravenous use of the prescription opioid pain reliever Opana ER. Initial cases were reported to the Food and Drug Administration by the manufacturer. The FDA contacted the CDC to discuss further investigation on October 5. The FDA issued an alert regarding the issue on October 11.

As of October 16, 2012, case-finding efforts by the TN DOH had uncovered a total of 10 cases resident in TN. A case was defined as hemolytic anemia combined with thrombocytopenia (platelet count <50,000/microliter) in the absence of any obvious explanation such as advanced cancer or systemic infection. The first case was diagnosed on April 16, the index cluster in mid-July, and the most recent case on October 4. All case patients were non-pregnant women 20 to 50 years of age. All were hospitalized, and 9 were treated with plasmapheresis. At least 5 patients have had recurrent episodes, but no deaths have occurred. Nine of the 10 patients reported IV use of Opana ER to the TN DOH. The tenth patient reported such use to clinical staff during hospitalization. Case patients all had a history of chronic IV use of Opana ER for nonmedical purposes up until 1-2 days prior to diagnosis. Most patients did not have a prescription for Opana ER and obtained the drug from other, undisclosed sources. The TN DOH is conducting a case-control study.

Background on TTP and Opana ER

TTP is an uncommon but serious illness, with an incidence of approximately 1 per 100,000 per year and a high case-fatality rate if not treated. Fewer than 15% of TTP cases can be attributed to specific exposures, with quinine and anti-platelet drugs being the primary substances responsible. Drugs are thought to cause TTP by an immune-mediated mechanism or by direct toxicity. Abnormally low levels of ADAMST13 are found in some but not all cases. Most cases of drug-associated TTP occur in women.

Opana ER is an extended-release formulation of oxymorphone, a schedule II prescription opioid pain reliever manufactured by U.S.-based Endo Pharmaceuticals, Inc. Oxymorphone is roughly three times as potent as oral morphine. Opana ER is approved for the relief of moderate to severe pain in patients requiring continuous, around-the-clock opioid treatment for an extended period of time. Opana ER has been available in the U.S. in pill form for oral use since 2006. In the fourth quarter of 2011, 226,000 prescriptions for Opana ER were written in the US, as compared with 1,279,000 prescriptions for OxyContin.

A new formulation of Opana ER designed to be more difficult to abuse came on the market in February, 2012 and has gradually replaced the original formulation. The new formulation was designed to prevent pulverizing the pills or dissolving them for injection. The new formulation contains some inactive ingredients not found in the original formulation, including polyethylene oxide (PEO), polyvinyl alcohol, and talc.

Although Opana ER is prescribed less frequently than other extended-release opioid pain relievers such as OxyContin, it is popular among people who abuse prescription drugs. The Drug Enforcement Administration labeled oxymorphone as a drug of concern in 2011 due to reports of increased abuse. People who use Opana ER nonmedically might refer to the pills as “panda bears,” “stop signs,” or “octagons.”

Recommendations for Clinicians

The extent of this problem is not clear because there is no requirement to report such cases and because IV drug use might not be suspected or reported among patients with TTP. No cases of TTP related to oral use of Opana ER have been reported, and nothing indicates that use of Opana ER as prescribed presents a risk of TTP. However, in the interim:

A. Clinicians treating patients with TTP of unknown etiology should:

    1. Ask them about intravenous drug use.

        a. Patients who report IV drug use should be asked about the specific drugs injected.

    2. Perform a urine drug test.

        a. A negative drug test is not definitive because the interval between the critical drug use and diagnosis might be greater than the time during which a drug can be detected in the urine, which is probably not more than 4 days in the case of opioids.

    3. Request a copy of the patient’s prescriptions for controlled substances from the state prescription drug monitoring program to determine who has prescribed them Opana ER.

B. Clinicians treating patients with TTP who report IV use of Opana ER should:

    1. Counsel them regarding the risks of continued IV drug use, including blood-borne infections, fatal overdose, and TTP

    2. Refer them to substance abuse treatment programs in their community. Substance abuse treatment facilities can be located at: http://www.samhsa.gov/treatment/index.aspx

    3. Notify other clinicians who have prescribed the patient Opana ER of the diagnosis of TTP and the reported association with that drug

4. For patients who report IV use of Opana ER since February, 2012, report the case to your state health department for surveillance purposes.

C. Clinicians who are prescribing Opana ER for pain should not assume that its new formulation, designed to be more difficult to inject, will entirely prevent intravenous administration for nonmedical purposes.

Recommendations for Health Departments

Health Departments should de-identify information on case patients and transmit reports to the Centers for Disease Control and Prevention for surveillance purposes. A report template is available from and reports should be sent to: Len Paulozzi, MD, lbp4@cdc.gov.

CDC Case Definition

The current case definition is a diagnosis of TTP since February 1, 2012 in a person who had used drugs intravenously for nonmedical reasons.

Additional Information

FDA drug alert: http://www.fda.gov/Drugs/DrugSafety/ucm322432.htm
DEA drug alert: http://www.deadiversion.usdoj.gov/drugs_concern/oxymorphone.pdf
EpiX announcement: